Amendments to the Drawings:

The three attached replacement sheets containing new corrected drawings replace Figures 6A, 6B, 6C and 6D filed on September 12, 2001 and April 19, 2004. The changes in new corrected Figures 6A, 6B and 6C over original Figure 6 as filed on June 12, 2001 are shown in the three annotated sheets, which introduces the SEQ ID Nos. directly in the figure.

Attachment: Three (3) Replacement Sheets containing Figures 6A, 6B and 6C.
Three (3) Annotated Sheets Showing Changes in Figures 6A, 6B and 6C over original Figure 6 as filed.

REMARKS

The Examiner has required new corrected drawings in a communication dated August 25, 2004. Specifically, the Examiner stated that:

> the sequences depicted in Figures 6A-6D do not correspond to the description of Figure 6 in the specification. In particular, while the description of Figure 6 recites "(SEQ ID Nos: 6-25, 20, 21, 26-43, 65, 66, 44-63, 67, 64 respectively)," a review of the sequences of Figures 6A-6D (as compared to Applicant's Sequence Listing) reveals that this order does not in fact correspond to the order of the sequences depicted in proposed Figures 6A-6D.

Accordingly, in response Applicants submit new corrected Figures 6A, 6B and 6C, contained in the three Replacement Sheets of drawings, which replace the drawings submitted on September 12, 2001. Changes in the new corrected Figures 6A, 6B and 6C over original Figure 6 as filed on June 12, 2001 are shown in the three Annotated Sheets Showing Changes. The amendment over original Figure 6 as filed has been made merely to introduce the SEQ ID Nos. directly in the figure, which eliminates the confusion in the order of the sequences that was noted by the Examiner.

Since the SEQ ID Nos. are now directly contained in Figures 6A-6C, Applicants have amended the specification to delete the references to SEQ ID Nos. in the figure caption and to update reference to Figures 6A-6C. No new matter has been added with this amendment. Applicants also submit a Sequence Listing which reflects the SEQ ID Nos. in the new corrected drawings, in compliance with 37 C.F.R. §§ 1.821 through 1.825.

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the instant application.

Respectfully submitted,

Date: October 25, 2004

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Enclosure

FIGURE 6A

1. 'A' Allele, CYP2D6'3, A21337 deletion, Frameshift resulting in zero enzyme activity

	2637	
SEQ ID NO:6	5'- GCTAACTGAGCACAGGATGACC -3' NH2	CYPwt(+)A2624, 22mer,54%GC, Tm=63-64C
SEQ ID NO:7	5'- GCTAACTGAGCACAGGATGACC(A)30 -3' NH2	CYPwt(+)A2624 (A)30-3'NH2
SEQ ID NO:8	5'- CTAACTGAGCACAGGATGACC(A)30 -3' NH2	CYPwt(+)A2625 (A)30-3'NH2
SEQ ID NO:9	5'- CTAACTGAGCACAGGATGAC(A)30 -3' NH2	CYPwt(+)A2625b (A)30-3'NH2
SEQ ID NO:10	5'- GCTAACTGAGCAC-GGATGACC -3'NH2	CYPmut(+)A2624,21 mer,57%GC, Tm=61-63C
SEQ ID NO:11	5'- GCTAACTGAGCAC-GGATGACC(A)30 -3' NH2	CYPmut(+)A2624 (A)30-3'NH2
SEQ ID NO:12	5'- CTAACTGAGCAC-GGATGACC(A)30 -3' NH2	CYPmut(+)A2625 (A)30-3'NH2
SEQ ID NO:13	5'- CTAACTGAGCAC-GGATGAC(A)30 -3' NH2	CYPmut(+)A2625b(A)30-3'NH2
	|-2612	
SEQ ID NO:14	5'- GCTGGATGAGCTGCTAACTGAGCACAGGATGACCTGGGACCCAGCCCAGCC -3'	Wild Type(+)
SEQ ID NO:15	5'- GCTGGATGAGCTGCTAACTGAGCAC-GGATGACCTGGGACCCAGCCCAGCC -3'	Mut(+)

2. 'B' Allele, CYP2D6*4, G1934A, Spliceing defect resulting in zero enzyme activity

A. wt Probe - CYPwt(-)B1922 (C/A to mut at base 5) & CYPmut(+)B1922 (A/C to mut at base 13)

	1934	
SEQ ID NO:16	NH2 3'- GAGGGTGGGGGTCCTGC -5'	CYPwt(-)B1922, 17mer,76%GC, Tm=66C
SEQ ID NO:17	5'- CTCCCACCCCCAGGACG -3'NH2	CYPwt(+)B1922-Target
SEQ ID NO:18	5'- CTCCCACCCCCAAGACG -3' NH2	CYPmut(+)B1922, 17mer,71%GC, Tm=58-60C
SEQ ID NO:19	NH2 3'- GAGGGTGGGGGTTCTGC -5'	CYPmut(-)B1922- Target
	|-1909	
SEQ ID NO:20	5' - CCCTTACCCGCATCTCCCACCCCCAGGACGCCCCTTTCGCCCCAACGGTCT -3'	WildType(+)
SEQ ID NO:21	5 '- CCCTTACCCGCATCTCCCACCCCCAAGACGCCCCTTTCGCCCCAACGGTCT -3'	Mut(+)

B. CYPwt(-)B1930 (C/A to mut at base 13) and CYPmut(+)B1930 (A/C to wt at base 5)

SEQ ID NO:22	NH2 3'- GGGTCCTGCGGGGAAAG -5'	CYPwt(-) B1930,17mer,71%GC, Tm=56C
SEQ ID NO:23	NH2 3'- (A)30GGGTCCTGCGGGGAAAG -5'	CYPwt(-) B1930(A)30-3'NH2
SEQ ID NO:24	5'- CCCAAGACGCCCCTTTC -3' NH2	CYPmut(+)B1930, 17mer,65%GC,Tm=54C
SEQ ID NO:25	5'- CCCAAGACGCCCCTTTC(A)30 -3' NH2	CYPmut(+)B1930 (A)30-3'NH2
	|-1909	
SEQ ID NO:26	5'- CCCTTACCCGCATCTCCCACCCCCAGGACGCCCCTTTCGCCCCAACGGTCT -3'	Wild Type(+)
SEQ ID NO:27	5'- CCCTTACCCGCATCTCCCACCCCCAAGACGCCCCTTTCGCCCCAACGGTCT -3'	Mut(+)

added

added

FIGURE 6B

3. 'C' Allele, CYP2D6*9, G2702-A2704 deletion, decreased enzyme activity

```
                                                |-2702
SEQ ID NO:28                5'- GCAGAGATGGAGAAGGTGAGAG -3'NH2              CYPwt(+)C2691, 22mer,55%GC, Tm=60C
SEQ ID NO:29                5'- GCAGAGATGGAGAAGGTGAGAG(A)30 -3' NH2        CYPwt(+)C2691 (A)30-3'NH2
SEQ ID NO:30                 5'- CAGAGATGGAGAAGGTGAGAG(A)30 -3' NH2        CYPwt(+)C2692 (A)30-3'NH2
SEQ ID NO:31                5'- GCAGAGATGGA---GGTGAGAGTG -3' NH2           CYPmut(+)C2691, 21mer, 57%GC, Tm=60C
SEQ ID NO:32                5'- GCAGAGATGGA---GGTGAGAGTG(A)30 -3' NH2      CYPmut(+)C2691 (A)30-3'NH2
SEQ ID NO:33                 5'- CAGAGATGGA---GGTGAGAGTG(A)30 -3' NH2      CYPmut(+)C2692 (A)30-3'NH2
          |-2676
SEQ ID NO:34  3'- TGACTCCGGAAGGACCGTCTCTACCTCTTCCACTCTCACCGACGGTGCCAC -5'   Wild Type(-)
SEQ ID NO:35  3'- TGACTCCGGAAGGACCGTCTCTACCT---CCACTCTCACCGACGGTGCCAC -5'   Mut (-)
```

4. 'E' Allele, CYP2D6*7, A3023C, H324P amino acid change results in zero enzyme activity

A. wt Probe - CYPwt(-)E3009 (T/C to mut at base 5) & CYPmut(+)E3009 (C/A to wt at base 15)

```
                                    3023
SEQ ID NO:36          NH2 3'- CGAGTACTAGGATGTAGGC -5'                       CYPwt(-)E3009, 19mer,53%GC, Pred Tm=57
SEQ ID NO:37     NH2 3'- (A)30CGAGTACTAGGATGTAGGC -5'                       CYPwt(-) E3009(A)30-3'NH2
SEQ ID NO:38             5'- GCTCATGATCCTACCTCCG -3'NH2                     CYPmut(+)E3009,19mer,58%GC,Pred Tm=59C
SEQ ID NO:39             5'- GCTCATGATCCTACCTCCG(A)30 -3'NH2                CYPmut(+) E3009(A)30-3'NH2
          |-2998
SEQ ID NO:40  5'- TGGGGCCTCCTGCTCATGATCCTACATCCGGATGTGCAGC|GTGAGCCCATC -3'          Wild Type(+)
SEQ ID NO:41  5'- TGGGGCCTCCTGCTCATGATCCTACCTCCGGATGTGCAGC|GTGAGCCCATC -3'          Mut(+)
                                                          |-3038-Intron Start
```

B. CYPwt(-)E3018 (T/C to mut at base 14) and CYPmut(+)E3018 (C/T to wt at base 6)

```
SEQ ID NO:42                NH2 3'- GGATGTAGGCCTACACGTC -5'                CYPwt(-)E3018,19mer,58%GC,Tm=60
SEQ ID NO:43                    5'- CCTACATCCGGATGTGCAG -3'                CYPwt(+)E3018- Target
SEQ ID NO:44                    5'- CCTACCTCCGGATGTGCAG -3' NH2            CYPmut(+)E3018,19mer,63%GC,Tm=62C
SEQ ID NO:45                    3'- GGATGGAGGCCTACACGTC -5'                CYPmut(-) E3018- Target
          |-2998
SEQ ID NO:46  5'- TGGGGCCTCCTGCTCATGATCCTACATCCGGATGTGCAGC|GTGAGCCCATC -3'     Wild Type(+)
SEQ ID NO:47  5'- TGGGGCCTCCTGCTCATGATCCTACCTCCGGATGTGCAGC|GTGAGCCCATC -3'     Mut(+)
                                                          |-3038-Intron Start
```

added

added

FIGURE 6C

5. 'G' Allele, CYP2D6*8, G1846T, Stop codon, zero enzyme activity

added

SEQ ID NO:48	5'- CACTCCGGTGGGTGATGG(A)30 -3' NH2 (1846)	CYPwt(+)G1840(A)30-3'NH2,18mer,67%GC, Tm=60
SEQ ID NO:49	NH2 3'- (A)30GTGAGGCCACCCACTACC -5'	CYPwt(-) G1840(A)30-3'NH2
SEQ ID NO:50	5'- CACTCCTGTGGGTGATGG(A)30 -3' NH2	CYPmut(+)G1840(A)30-3'NH2,18mer, 61%GC, Tm=57
SEQ ID NO:51	5'- GTGCCGCCTTCGCCACTCC|GGTGGGTGATGGGCAGAAGGGCACAAAGCGGG -3'	
SEQ ID NO:52	5'- GTGCCGCCTTCGCCACTCC|TGTGGGTGATGGGCAGAAGGGCACAAAGCGGG -3'	
	Exon 3 end-|-1846	

6. 'T' Allele, CYP2D6*6, T1795 deletion, Frameshift resulting in zero enzyme activity

added

SEQ ID NO:53	5'- GCTGGAGCAGTGGGTGAC -3' NH2	CYPwt(+)T1785, 18mer,67%GC, Trn=59-61C
SEQ ID NO:54	5'- GCTGGAGCAGTGGGTGAC(A)30 -3' NH2	CYPwt(+)T1785 (A)30-3'NH2
SEQ ID NO:55	5'- CTGGAGCAGTGGGTGAC(A)30 -3' NH2	CYPwt(+)T1786 (A)30-3'NH2
SEQ ID NO:56	5'- GCTGGAGCAG-GGGTGAC -3' NH2	CYPmut(+)T1785, 17mer,71 %GC, Tm=58-60C
SEQ ID NO:57	5'- GCTGGAGCAG-GGGTGAC(A)30 -3' NH2	CYPmut(+)T1785 (A)30-3'NH2
SEQ ID NO:58	5'- CTGGAGCAG-GGGTGAC(A)30 -3' NH2	CYPmut(+)T1786 (A)30-3'NH2
	|-1773	
SEQ ID NO:59	5'-GGGCAAGAAGTCGCTGGAGCAGTGGGTGACCGAGGAGGCCGCCTGCCT -3'	Wild Type(+)
SEQ ID NO:60	5'-GGGCAAGAAGTCGCTGGAGCAG-GGGTGACCGAGGAGGCCGCCTGCCT -3'	Mut(+)

7. 2D6/2D7/2D8 Controls - The 2D6/7/8 probes were designed in the 1600 region of the 2D6 gene. The purpose of the designs was to find region somewhere between the PCR primers were it would be easy to discriminate between 2D6 and its two pseudogenes, 2D7 and 2D8. The purpose of the designs is to demonstrate that the PCR amplicon is from the 2D6 gene, not one of the pseudogenes.

added

SEQ ID NO:61	5'- GACCAGGGGGAGC-ATAGG(A)30-3' NH2	CYP2D6wt(+)1607(A)30-3'NH2
SEQ ID NO:62	5'- GACCTTGTGGAGCGCCAG(A)30-3' NH2	CYP2D7wt(+)1607(A)30-3'NH2
SEQ ID NO:63	5'- GACCAGGAAAAGC-ACAGG(A)30-3' NH2	CYP2D8wt(+)1607(A)30-3'NH2
SEQ ID NO:64	5'- GACCAGGAAAAGC-ACAGGG(A)30-3' NH2	CYP2D8wt(+) 1607b (A)30-3'NH2
	|-1603	
SEQ ID NO:65	5' - GGGAGACCAGGGGGAGC-ATAGGGTTGGAGTGGGTGGT -3'	2D6(+)
SEQ ID NO:66	5' - GGGAGACCTTGTGGAGCGCCAGGGTTGGAGTGGGTGGC -3'	2D7(+)
SEQ ID NO:67	5' - GGGAGACCAGGAAAAGC-ACAGGGTTGGAGTGGGCGGC -3'	2D8(+)

8. Pos/Neg Control probes- These probes were designed as true positive and negative control probes. They consist of the same semi-random sequence, with the positive control probe having a 5' Biotin.

added

SEQ ID NO:68	5' Biotin- ATCATTCCAATCATCCATATCATC(A)25 -3' NH2	CYP(+)ran(A)25-5'Biotin,3'NH2
SEQ ID NO:69	5'- ATCATTCCAATCATCCATATCATC(A)25 -3' NH2	CYP(+)ran(A)25-3'NH2